

Description of Additional Supplementary Files

Supplementary Data 1. CRISPR sgRNA sequences used for the *PARP1* focused mutagenesis screen.

Supplementary Data 2. Translated protein alignments for the *PARP1* mutants isolated in the HeLa screen.

Supplementary Data 3. Ion Torrent sequencing mutation calls for the *PARP1* mutants isolated in the HeLa screen.

Supplementary Data 4. *PARP1* mutations in talazoparib-resistant SUM149 clones TR1 and TR2.

Supplementary Data 5. Guide sequences used in the *PARP1* dense library.

Supplementary Data 6. Primer sequences with Ion Torrent adapters for genotyping mutations in the dense *PARP1* mutagenesis screen.

Supplementary Data 7. *PARP1* mutations identified in talazoparib-resistant SUM149 *PARP1-tagGFP2* cells in the dense mutagenesis screen.

Supplementary Data 8. Primer and sgRNA target sequences used in this study.

Supplementary Data 9. Antibodies and working dilutions used in this study.